Have researchers found a new treatment for sepsis?

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Sepsis, or septicaemia, is a devastating disease that is difficult to diagnose early and for which treatment options are limited. The number of deaths from sepsis exceeds those from lung cancer, and from breast and bowel cancer combined.

Sepsis can affect any age group and is the leading cause of death in Intensive Care: it is estimated that 37,000 people die from severe sepsis in the UK each year with annual NHS costs exceeding £1.5billion.

Sepsis has until recently been under-recognised and despite advances in understanding the biological processes involved, there is still no effective treatment beyond supportive therapy.

Professor David Lambert and Dr Jonathan Thompson of the Department of Cardiovascular Sciences at the University of Leicester have published two collaborative research papers indicating that a newly discovered receptor in the body – similar to the receptors for endorphins or for morphine - might be important in the body's response to sepsis, which could be the key to unlocking a new treatment in the future.

This new receptor is called the 'nociceptin receptor' and the natural substance that activates it is called nociceptin.

The body's initial response to sepsis is to produce an intense reaction from the immune system to fight the infection. This first involves activation of white blood cells, stress hormones and other substances,

known as 'inflammatory mediators', which cause inflammation.

It has already been found that nociceptin is involved in inflammation; it affects how white blood cells work. This suggests strongly that nociceptin has an important role in the body's response to inflammation and sepsis. Their theory, which they have explored in both research papers, is that nociceptin makes inflammation or sepsis worse; by blocking the nociceptin system, the symptoms of sepsis could be reduced, which could lead to new treatments.

In the first of the two papers Professor Lambert, as part of a collaboration with Dr Zoë Brookes at the University of Sheffield and Dr Girolamo Calo and Dr Remo Guerrini at the University of Ferrara, has shown for the first time using fluorescent chemistry - which was designed in Ferrara - that nociceptin receptors are found on blood vessels with no nerve supply and that in a laboratory model of sepsis, blocking these receptors is protective. This work was funded by British Journal of Anaesthesthia / Royal College of Anaesthetists and Anaesthetic Research Society.

In the second paper, funded by the Association of Anaesthetists of Great Britain and Ireland and British Journal of Anaesthesia / Royal College of Anaesthetists, Dr Thompson and Professor Lambert have discovered that nociceptin levels in the bloodstream are elevated in patients with sepsis in Intensive Care, demonstrating that nociceptin activation might be important in critically ill patients suffering from sepsis.

Sepsis remains a leading cause of admission to Intensive Care Units, with high mortality, costs, and long-term morbidity in those who survive. The incidence of severe sepsis has increased over the last decade, making the discovery of new treatments highly desirable.

Dr Jonathan Thompson said: "Sepsis is a major health problem for the

NHS that has often been under-recognised. It can be rapidly fatal, especially if not diagnosed and treated early, because inflammation can spread and affect many different organs in the body.

"Clinicians are making progress in the early recognition and treatment of sepsis, but we have no specific drugs that effectively stop the spread of inflammation, or the biological processes involved. We have found that nociceptin, a chemical similar to endorphins produced in the body, is increased in inflammation and sepsis.

"This suggests that drugs which block the nociceptin receptor could dampen the widespread inflammation that occurs in sepsis, and improve outcome. More work is needed, but these drugs are being developed. If they are effective then we could potentially save many lives."

Professor David Lambert added: "I am particularly excited by these findings as they translate many years of laboratory work into a possible target for this disease."

More information: The first paper, 'The Nociceptin/Orphanin FQ Receptor Antagonist UFP-101 Reduces Microvascular Inflammation to Lipopolysaccharide In Vivo', can be accessed at the following link: www.plosone.org/article/info%3Adoi%2F10.1371%2Fjournal.pone.0074943

The second paper, 'The Nociceptin/Orphanin FQ System Is Modulated in Patients Admitted to ICU with Sepsis and after Cardiopulmonary Bypass', can be accessed at the following link: www.plosone.org/article/info%3Adoi%2F10.1371%2Fjournal.pone.0076682

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